What is claimed is:

1. An isolated nucleic acid encoding a $GABA_BR2$ polypeptide.

2. The nucleic acid of claim 1, wherein the nucleic acid is DNA.

3. The DNA of claim 2, wherein the DNA is cDNA.

4. The DNA of claim 2, wherein the DNA is genomic DNA.

5. The nucleic acid of claim 1, wherein the nucleic acid is RNA.

6. The nucleic acid of claim 1, wherein the nucleic acid encodes a mammalian $GABA_BR2$ polypeptide.

7. The nucleic acid of claim 1, wherein the nucleic acid encodes a rat $GABA_BR2$ polypeptide.

8. The nucleic acid of claim 1, wherein the nucleic acid encodes a human $GABA_BR2$ polypeptide.

9. The nucleic acid of claim 6, wherein the nucleic acid encodes a polypeptide characterized by an amino acid sequence in the transmembrane regions which has an identity of 90% or higher to the amino acid sequence in the transmembrane regions of the human $GABA_BR2$ polypeptide shown in Figures 5A-5D.

10. The nucleic acid of claim 6, wherein the nucleic acid encodes a mammalian $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as does the $GABA_BR2$ polypeptide encoded by the plasmid BO-55 (ATCC Accession No. 209104).

11. The nucleic acid of claim 7, wherein the nucleic acid encodes a rat $GABA_BR2$ polypeptide which has an amino acid sequence encoded by the plasmid BO-55 (ATCC Accession No. 209104).

12. The nucleic acid of claim 7, wherein the nucleic acid encodes a rat $GABA_BR2$ polypeptide having substantially the same amino acid sequence as the amino acid sequence shown in Figures 4A-4D (Seq. ID No. 4).

13. The nucleic acid of claim 7, wherein the rat $GABA_BR2$ polypeptide has an amino acid sequence which comprises the amino acid sequence shown in Figures 4A-4D (Seq. ID No. 4).

14. The nucleic acid of claim 6, wherein the nucleic

acid encodes a mammalian $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as does the $GABA_BR2$ polypeptide encoded by the plasmid pEXJT3T7-hGABAB2 (ATCC Accession No.).

15. The nucleic acid of claim 8, wherein the human $GABA_BR2$ polypeptide comprises an amino acid sequence substantially the same as the amino acid sequence encoded by plasmid pEXJT3T7-hGABAB2 (ATCC Accession No.).

16. The nucleic acid of claim 8, wherein the human $GABA_BR2$ polypeptide comprises an amino acid sequence substantially the same as the amino acid sequence in Figures 23A-23D (Seq. ID No. 47).

17. The nucleic acid of claim 8, wherein the human $GABA_BR2$ polypeptide has an amino acid sequence which comprises the sequence shown in Figures 23A-23D (Seq. ID No. 47).

18. A purified $GABA_BR2$ protein.

19. A vector comprising the nucleic acid of claim 1.

20. A vector comprising the nucleic acid of claim 8.

21. A vector of claim 19 adapted for expression in a

bacterial cell which comprises the regulatory elements necessary for expression of the nucleic acid in the bacterial cell operatively linked to the nucleic acid encoding a $GABA_BR2$ polypeptide so as to permit expression thereof.

22. A vector of claim 19 adapted for expression in an amphibian cell which comprises the regulatory elements necessary for expression of the nucleic acid in the amphibian cell operatively linked to the nucleic acid encoding a $GABA_BR2$ polypeptide so as to permit expression thereof.

23. A vector of claim 19 adapted for expression in a yeast cell which comprises the regulatory elements necessary for expression of the nucleic acid in the yeast cell operatively linked to the nucleic acid encoding a $GABA_BR2$ polypeptide so as to permit expression thereof.

24. A vector of claim 19 adapted for expression in an insect cell which comprises the regulatory elements necessary for expression of the nucleic acid in the insect cell operatively linked to the nucleic acid encoding the $GABA_BR2$ polypeptide so as to permit expression thereof.

25. A vector of claim 24 which is a baculovirus.

26. A vector of claim 19 adapted for expression in a mammalian cell which comprises the regulatory

elements necessary for expression of the nucleic acid in the mammalian cell operatively linked to the nucleic acid encoding a $GABA_BR2$ polypeptide so as to permit expression thereof.

27. A vector of claim 19 wherein the vector is a plasmid.

28. The plasmid of claim 27 designated BO-55 (ATCC Accession No. 209104).

29. The plasmid of claim 27 designated pEXJT3T7-hGABAB2 (ATCC Accession No.).

30. A method of detecting a nucleic acid encoding a $GABA_BR2$ polypeptide, which comprises contacting the nucleic acid with a probe comprising at least 15 nucleotides, which probe specifically hybridizes with the nucleic acid encoding the $GABA_BR2$ polypeptide, wherein the probe has a unique sequence, which sequence is present within one of the two strands of the nucleic acid encoding the $GABA_BR2$ polypeptide contained in plasmid BO-55, and detecting hybridization of the probe to the nucleic acid.

31. A method of detecting a nucleic acid encoding a $GABA_BR2$ polypeptide, which comprises contacting the nucleic acid with a probe comprising at least 15 nucleotides, which probe specifically

hybridizes with the nucleic acid encoding the $GABA_BR2$ polypeptide, wherein the probe has a unique sequence, which sequence is present within (a) the nucleic acid sequence shown in Figures 22A-22D (Seq. ID No. 46) or (b) the reverse complement to the nucleic acid sequence shown in Figures 22A-22D (Seq. ID No. 46), and detecting hybridization of the probe to the nucleic acid.

32. A method of detecting a nucleic acid encoding a $GABA_BR2$ polypeptide, which comprises contacting the nucleic acid with a probe comprising at least 15 nucleotides, which probe specifically hybridizes with the nucleic acid encoding the $GABA_BR2$ polypeptide, wherein the probe has a unique sequence, which sequence is present within one of the two strands of the nucleic acid encoding the $GABA_BR2$ polypeptide contained in plasmid pEXJT3T7-hGABAB2, and detecting hybridization of the probe to the nucleic acid.

33. A method of detecting a nucleic acid encoding a $GABA_BR2$ polypeptide, which comprises contacting the nucleic acid with a probe comprising at least 15 nucleotides, which probe specifically hybridizes with the nucleic acid encoding the $GABA_BR2$ polypeptide, wherein the probe has a unique sequence, which sequence is present within (a) the nucleic acid sequence shown in Figures 3A-3D (Seq. ID No. 3) or (b) the reverse complement to the nucleic acid sequence shown in Figures 3A-3D (Seq. ID No. 3), and detecting hybridization of the probe to the nucleic acid.

34. The method of any one of claims 30 to 33, wherein the nucleic acid is DNA.

35. The method of any one of claims 30 to 33, wherein the nucleic acid is RNA.

36. The method of any one of claims 30 to 33, wherein the probe comprises at least 15 nucleotides complementary to a unique segment of the sequence of the nucleic acid molecule encoding the $GABA_BR2$ polypeptide.

37. A method of detecting a nucleic acid encoding a $GABA_BR2$ polypeptide, which comprises contacting the nucleic acid with a probe comprising a nucleic acid of at least 15 nucleotides which is complementary to the antisense sequence of a unique segment of the sequence of the nucleic acid encoding the $GABA_BR2$ polypeptide, and detecting hybridization of the probe to the nucleic acid.

38. A method of inhibiting translation of mRNA encoding a $GABA_BR2$ polypeptide which comprises contacting such mRNA with an antisense oligonucleotide having a sequence capable of specifically hybridizing to the mRNA of claim 5, so as to prevent translation of the mRNA.

39. A method of inhibiting translation of mRNA

encoding a $GABA_BR2$ polypeptide which comprises contacting such mRNA with an antisense oligonucleotide having a sequence capable of specifically hybridizing to the genomic DNA of claim 4.

40. The method of claim 38 or 39, wherein the oligonucleotide comprises chemically modified nucleotides or nucleotide analogues.

41. An isolated antibody capable of binding to a $GABA_BR2$ polypeptide encoded by the nucleic acid of claim 1.

42. The antibody of claim 41, wherein the $GABA_BR2$ polypeptide is a human $GABA_BR2$ polypeptide.

43. An antibody capable of competitively inhibiting the binding of the antibody of claim 41 to a $GABA_BR2$ polypeptide.

44. An antibody of claim 41, wherein the antibody is a monoclonal antibody.

45. A monoclonal antibody of claim 44 directed to an epitope of a $GABA_BR2$ polypeptide present on the surface of a $GABA_BR2$ polypeptide expressing cell.

46. A method of claim 38 or 39, wherein the oligonucleotide is coupled to a substance which inactivates mRNA.

47. A method of claim 46, wherein the substance which inactivates mRNA is a ribozyme.

48. A pharmaceutical composition which comprises an amount of the antibody of claim 41 effective to block binding of a ligand to the $GABA_BR2$ polypeptide and a pharmaceutically acceptable carrier.

49. A transgenic, nonhuman mammal expressing DNA encoding a $GABA_BR2$ polypeptide of claim 1.

50. A transgenic, nonhuman mammal comprising a homologous recombination knockout of the native $GABA_BR2$ polypeptide.

51. A transgenic, nonhuman mammal whose genome comprises antisense DNA complementary to DNA encoding a $GABA_BR2$ polypeptide of claim 1 so placed as to be transcribed into antisense mRNA which is complementary to mRNA encoding such $GABA_BR2$ polypeptide and which hybridizes to such mRNA encoding such $GABA_BR2$ polypeptide, thereby reducing its translation.

52. The transgenic, nonhuman mammal of claim 49 or 50, wherein the DNA encoding the $GABA_BR2$ polypeptide additionally comprises an inducible promoter.

53. The transgenic, nonhuman mammal of claim 49 or 50, wherein the DNA encoding the $GABA_BR2$ polypeptide additionally comprises tissue specific regulatory elements.

54. A transgenic, nonhuman mammal of any one of claims 49, 50 or 51, wherein the transgenic, nonhuman mammal is a mouse.

55. A method of detecting the presence of a $GABA_BR2$ polypeptide on the surface of a cell which comprises contacting the cell with the antibody of claim 41 under conditions permitting binding of the antibody to the polypeptide, detecting the presence of the antibody bound to the cell, and thereby detecting the presence of a $GABA_BR2$ polypeptide on the surface of the cell.

56. A method of preparing the purified $GABA_BR2$ polypeptide of claim 18 which comprises:

a. inducing cells to express a $GABA_BR2$ polypeptide;

b. recovering the polypeptide so expressed from

the induced cells; and

c. purifying the polypeptide so recovered.

57. A method of preparing the purified $GABA_BR2$ polypeptide of claim 18 which comprises:

a. inserting a nucleic acid encoding the $GABA_BR2$ polypeptide into a suitable vector;

b. introducing the resulting vector in a suitable host cell;

c. placing the resulting cell in suitable condition permitting the production of the $GABA_BR2$ polypeptide;

d. recovering the polypeptide produced by the resulting cell; and

e. isolating or purifying the polypeptide so recovered.

58. A $GABA_BR1/R2$ receptor comprising two polypeptides, one of which is a $GABA_BR2$ polypeptide and another of which is a $GABA_BR1$ polypeptide.

59. A method of forming a $GABA_BR1/R2$ receptor which comprises inducing cells to express both a $GABA_BR1$ polypeptide and a $GABA_BR2$ polypeptide.

60. An antibody capable of binding to a $GABA_BR1/R2$ receptor, wherein the $GABA_BR2$ polypeptide is encoded by the nucleic acid of claim 1.

61. The antibody of claim 60, wherein the $GABA_BR2$ polypeptide is a human $GABA_BR2$ polypeptide.

62. An antibody capable of competitively inhibiting the binding of the antibody of claim 60 to a $GABA_BR1/R2$ receptor.

63. An antibody of claim 60, wherein the antibody is a monoclonal antibody.

64. A monoclonal antibody of claim 63 directed to an epitope of a $GABA_BR1/R2$ receptor present on the surface of a $GABA_BR1/R2$ polypeptide expressing cell.

65. A pharmaceutical composition which comprises an amount of the antibody of claim 60 effective to block binding of a ligand to the $GABA_BR1/R2$ receptor and a pharmaceutically acceptable carrier.

66. A transgenic, nonhuman mammal expressing a $GABA_BR1/R2$ receptor, which is not naturally expressed by the mammal.

67. A transgenic, nonhuman mammal comprising a homologous recombination knockout of the native $GABA_BR1/R2$ receptor.

68. A transgenic, nonhuman mammal of claim 66 or 67, wherein the transgenic nonhuman mammal is a mouse.

69. A method of detecting the presence of a $GABA_BR1/R2$ receptor on the surface of a cell which comprises contacting the cell with the antibody of claim 60 under conditions permitting binding of the antibody to the receptor, detecting the presence of the antibody bound to the cell, and thereby detecting the presence of a $GABA_BR1/R2$ receptor on the surface of the cell.

70. A method of determining the physiological effects of varying levels of activity of $GABA_BR1/R2$ receptors which comprises producing a transgenic nonhuman mammal of claim 66 whose levels of $GABA_BR1/R2$ receptor activity vary due to the presence of an inducible promoter which regulates $GABA_BR1/R2$ receptor expression.

71. A method of determining the physiological effects of varying levels of activity of $GABA_BR1/R2$ receptors which comprises producing a panel of

transgenic nonhuman mammals of claim 66, each expressing a different amount of $GABA_BR1/R2$ receptor.

72. A method for identifying an antagonist capable of alleviating an abnormality, by decreasing the activity of a $GABA_BR1/R2$ receptor comprising administering a compound to the transgenic nonhuman mammal of claim 66 or 68, and determining whether the compound alleviates the physical and behavioral abnormalities displayed by the transgenic, nonhuman mammal, the alleviation of the abnormality identifying the compound as the antagonist.

73. An antagonist identified by the method of claim 72.

74. A pharmaceutical composition comprising an antagonist of claim 73 and a pharmaceutically acceptable carrier.

75. A method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a $GABA_BR1/R2$ receptor which comprises administering to a subject an effective amount of the pharmaceutical composition of claim 74, thereby treating the abnormality.

76. A method for identifying an agonist capable of alleviating an abnormality, by increasing the

activity of a $GABA_BR1/R2$ receptor comprising administering a compound to the transgenic nonhuman mammal of claim 66 or 68, and determining whether the compound alleviates the physical and behavioral abnormalities displayed by the transgenic, nonhuman mammal, the alleviation of the abnormality identifying the compound as the agonist.

77. An agonist identified by the method of claim 76.

78. A pharmaceutical composition comprising an agonist of claim 76 and a pharmaceutically acceptable carrier.

79. A method for treating an abnormality in a subject wherein the abnormality is alleviated by increasing the activity of a $GABA_BR1/R2$ receptor which comprises administering to a subject an effective amount of the pharmaceutical composition of claim 78, thereby treating the abnormality.

80. A cell which expresses on its surface a mammalian $GABA_BR1/R2$ receptor that is not naturally expressed on the surface of such cell.

81. A cell of claim 80, wherein the mammalian $GABA_BR1/R2$ receptor comprises two polypeptides, one of which is a $GABA_BR2$ polypeptide and another of which is a $GABA_BR1$ polypeptide.

82. A process for identifying a chemical compound which specifically binds to a $GABA_BR1/R2$ receptor which comprises contacting cells containing nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the $GABA_BR1/R2$ receptor.

83. A process for identifying a chemical compound which specifically binds to a $GABA_BR1/R2$ receptor which comprises contacting a membrane fraction from a cell extract of cells containing nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with the compound under conditions suitable for binding, and detecting specific binding of the chemical compound to the $GABA_BR1/R2$ receptor.

84. The process of claim 82 or 83, wherein the $GABA_BR1/R2$ receptor is a mammalian $GABA_BR1/R2$ receptor.

85. The process of claim 82 or 83, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by the plasmid BO-55 (ATCC Accession No. 209104).

86. The process of claim 82 or 83, wherein the

$GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same sequence as the amino acid sequence shown in Figures 23A-23D (Seq. ID No. 47).

87. The process of claim 82 or 83, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has the amino acid sequence shown in Figures 23A-23D (Seq. ID No. 47).

88. The process of claims 82 or 83, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by the plasmid pEXJT3T7-hGABAB2 (ATCC Accession No.).

89. The process of claim 82 or 83, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as the sequence shown in Figures 23A-23D (Seq. ID No. 47).

90. The process of claim 82 or 83, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has the sequence shown in Figures 23A-23D (Seq. ID No. 47).

91. The process of claim 89, wherein the compound is not previously known to bind to a $GABA_BR1/R2$ receptor.

92. A compound identified by the process of claim 91.

93. A process of claim 89, wherein the cell is an insect cell.

94. A process of claim 89, wherein the cell is a mammalian cell.

95. A process of claim 94, wherein the cell is nonneuronal in origin.

96. A process of claim 95, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell a mouse Y1 cell or LM(tk-) cell.

97. A process of claim 94, wherein the compound is not previously known to bind to a $GABA_B$R1/R2 receptor.

98. A compound identified by the process of claim 97.

99. A process involving competitive binding for identifying a chemical compound which specifically binds to a $GABA_B$R1/R2 receptor which comprises separately contacting cells expressing on their cell surface the $GABA_B$R1/R2 receptor, wherein such cells do not normally express the $GABA_B$R1/R2 receptor, with both the chemical compound and a

second chemical compound known to bind to the receptor, and with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the $GABA_BR1/R2$ receptor, a decrease in the binding of the second chemical compound to the $GABA_BR1/R2$ receptor in the presence of the chemical compound indicating that the chemical compound binds to the $GABA_BR1/R2$ receptor.

100. A process involving competitive binding for identifying a chemical compound which specifically binds to a human $GABA_BR1/R2$ receptor which comprises separately contacting a membrane fraction from a cell extract of cells expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with both the chemical compound and a second chemical compound known to bind to the receptor, and with only the second chemical compound, under conditions suitable for binding of both compounds, and detecting specific binding of the chemical compound to the $GABA_BR1/R2$ receptor, a decrease in the binding of the second chemical compound to the $GABA_BR1/R2$ receptor in the presence of the chemical compound indicating that the chemical compound binds to the $GABA_BR1/R2$ receptor.

101. A process of claim 99 or 100, wherein the $GABA_BR1/R2$ receptor is a mammalian $GABA_BR1/R2$ receptor.

102. The process of claim 101, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by plasmid BO-55 (ATCC Accession No. 209104).

103. The process of claim 99 or 100, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that shown in Figures 23A-23D (Seq. ID No. 47).

104. The process of claim 99 or 100, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has the amino acid sequence shown in Figures 23A-23D (Seq. ID No. 47).

105. The process of claim 99 or 100, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by plasmid pEXJT3T7-hGABAB2 (ATCC Accession No.).

106. The process of claim 99 or 100, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as the sequence shown in Figures 23A-23D (Seq. ID No. 47).

107. The process of claim 99 or 100, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide

which has the sequence shown in Figures 23A-23D (Seq. ID No. 47).

108. The process of claim 107, wherein the cell is an insect cell.

109. The process of claim 107, wherein the cell is a mammalian cell.

110. The process of claim 109, wherein the cell is nonneuronal in origin.

111. The process of claim 110, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell a mouse Y1 cell or LM(tk-) cell.

112. The process of claim 109, wherein the compound is not previously known to bind to a $GABA_BR1/R2$ receptor.

113. A compound identified by the process of claim 112.

114. A method of screening a plurality of chemical compounds not known to bind to a $GABA_BR1/R2$ receptor to identify a compound which specifically binds to the $GABA_BR1/R2$ receptor, which comprises

(a) contacting cells containing nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with a compound known to bind specifically to the $GABA_BR1/R2$ receptor;

(b) contacting the same cells as in step (a) with the plurality of compounds not known to bind specifically to the $GABA_BR1/R2$ receptor, under conditions permitting binding of compounds known to bind the $GABA_BR1/R2$ receptor;

(c) determining whether the binding of the compound known to bind specifically to the $GABA_BR1/R2$ receptor is reduced in the presence of the plurality of the compounds, relative to the binding of the compound in the absence of the plurality of compounds, and if the binding is reduced;

(d) separately determining the extent of binding to the $GABA_BR1/R2$ receptor of each compound included in the plurality of compounds, so as to thereby identify the compound or compounds present in such plurality of compounds which specifically binds to the $GABA_BR1/R2$ receptor.

115. A method of screening a plurality of chemical compounds not known to bind to a $GABA_BR1/R2$ receptor to identify a compound which specifically binds to the $GABA_BR1/R2$ receptor, which comprises

(a) contacting a membrane fraction extract from cells containing nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with a compound known to bind specifically to the $GABA_BR1/R2$ receptor;

(b) contacting the same membrane fraction as in step (a) with the plurality of compounds not known to bind specifically to the $GABA_BR1/R2$ receptor, under conditions permitting binding of compounds known to bind the $GABA_BR1/R2$ receptor;

(c) determining whether the binding of the compound known to bind specifically to the $GABA_BR1/R2$ receptor is reduced in the presence of the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds, and if the binding is reduced;

(d) separately determining the extent of binding to the $GABA_BR1/R2$ receptor of each compound included in the plurality of compounds, so as to thereby identify the compound or compounds present in such plurality of compounds which specifically binds to the $GABA_BR1/R2$ receptor.

116. A method of claim 114 or 115, wherein the $GABA_BR1/R2$ receptor is a mammalian $GABA_BR1/R2$

receptor.

117. A method of either of claim 114 or 115, wherein the cell is a mammalian cell.

118. A method of claim 117, wherein the mammalian cell is non-neuronal in origin.

119. The method of claim 118, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell, a CHO cell, a mouse Y1 cell or an NIH-3T3 cell.

120. A process for determining whether a chemical compound is a $GABA_BR1/R2$ receptor agonist which comprises contacting cells with the compound under conditions permitting the activation of the $GABA_BR1/R2$ receptor, and detecting an increase in $GABA_BR1/R2$ receptor activity, so as to thereby determine whether the compound is a $GABA_BR1/R2$ receptor agonist.

121. A process for determining whether a chemical compound is a $GABA_BR1/R2$ receptor antagonist which comprises contacting cells containing nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with the compound in the presence of a known $GABA_BR1/R2$ receptor agonist, under conditions permitting the activation of the $GABA_BR1/R2$ receptor, and

detecting a decrease in $GABA_BR1/R2$ receptor activity, so as to thereby determine whether the compound is a $GABA_BR1/R2$ receptor antagonist.

122. A process of claim 120 or 121, wherein the cells additionally express nucleic acid encoding GIRK1 and GIRK4.

123. A process of any one of claims 120, 121, or 122, wherein the $GABA_BR2$ receptor is a mammalian $GABA_BR2$ receptor.

124. A pharmaceutical composition which comprises an amount of a $GABA_BR1/R2$ receptor agonist determined to be an agonist by the process of claim 120 effective to increase activity of a $GABA_BR1/R2$ receptor and a pharmaceutically acceptable carrier.

125. A pharmaceutical composition of claim 124, wherein the $GABA_BR1/R2$ receptor agonist was not previously known.

126. A pharmaceutical composition which comprises an amount of a $GABA_BR1/R2$ receptor antagonist determined to be an antagonist the process of claim 121 effective to reduce activity of a $GABA_BR1/R2$ receptor and a pharmaceutically acceptable carrier.

127. A pharmaceutical composition of claim 126, wherein the $GABA_BR1/R2$ receptor antagonist was not previously known.

128. A process for determining whether a chemical compound activates a $GABA_BR1/R2$ receptor, which comprises contacting cells producing a second messenger response and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with the chemical compound under conditions suitable for activation of the $GABA_BR1/R2$ receptor, and measuring the second messenger response in the presence and in the absence of the chemical compound, a change in the second messenger response in the presence of the chemical compound indicating that the compound activates the $GABA_BR1/R2$ receptor.

129. The process of claim 128, wherein the second messenger response comprises potassium channel activation and the change in second messenger is an increase in the level of potassium current.

130. A process for determining whether a chemical compound inhibits activation of a $GABA_BR1/R2$ receptor, which comprises separately contacting cells producing a second messenger response and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with both the chemical compound and a second chemical compound known to activate the $GABA_BR1/R2$ receptor, and with

only the second chemical compound, under conditions suitable for activation of the $GABA_BR1/R2$ receptor, and measuring the second messenger response in the presence of only the second chemical compound and in the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the $GABA_BR1/R2$ receptor.

131. The process of claim 130, wherein the second messenger response comprises potassium channel activation and the change in second messenger response is a smaller increase in the level of inward potassium current in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

132. A process of any one of claims 128, 129, 130 or 131, wherein the $GABA_BR1/R2$ receptor is a mammalian $GABA_BR1/R2$ receptor.

133. The process of claim 132, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by the plasmid BO-55 (ATCC Accession No. 209104).

134. The process of claim 132, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that shown in Figures 4A-4D (Seq. ID No. 4).

135. The process of claim 132, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that shown in Figures 23A-23D (Seq. ID No. 47).

136. The process of claim 132, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has the sequence, shown in Figures 23A-23D (Seq. ID No. 47).

137. The process of claim 132, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by the plasmid pEXJT3T7-hGABAB2 (ATCC Accession No.).

138. The process of any one of claims 128-131, wherein the cell is an insect cell.

139. The process of any one of claims 128-131, wherein the cell is a mammalian cell.

140. The process of claim 139, wherein the mammalian cell is nonneuronal in origin.

141. The process of claim 140, wherein the nonneuronal cell is a COS-7 cell, CHO cell, 293 human embryonic kidney cell, NIH-3T3 cell or LM(tk-) cell.

142. The process of claim 139, wherein the compound was not previously known to activate or inhibit a $GABA_BR1/R2$ receptor.

143. A compound determined by the process of claim 142.

144. A pharmaceutical composition which comprises an amount of a $GABA_BR1/R2$ receptor agonist determined by the process of claim 128 or 129 effective to increase activity of a $GABA_BR1/R2$ receptor and a pharmaceutically acceptable carrier.

145. A pharmaceutical composition of claim 144, wherein the $GABA_BR1/R2$ receptor agonist was not previously known.

146. A pharmaceutical composition which comprises an amount of a $GABA_BR1/R2$ receptor antagonist determined by the process of claim 130 or 131 effective to reduce activity of a $GABA_BR1/R2$ receptor and a pharmaceutically acceptable carrier.

147. A pharmaceutical composition of claim 146, wherein

the $GABA_BR1/R2$ receptor antagonist was not previously known.

148. A method of screening a plurality of chemical compounds not known to activate a $GABA_BR1/R2$ receptor to identify a compound which activates the $GABA_BR1/R2$ receptor which comprises:

(a) contacting cells containing nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with the plurality of compounds not known to activate the $GABA_BR1/R2$ receptor, under conditions permitting activation of the $GABA_BR1/R2$ receptor;

(b) determining whether the activity of the $GABA_BR1/R2$ receptor is increased in the presence of the compounds, and if it is increased;

(c) separately determining whether the activation of the $GABA_BR1/R2$ receptor is increased by each compound included in the plurality of compounds, so as to thereby identify the compound or compounds present in such plurality of compounds which activates the $GABA_BR1/R2$ receptor.

149. The process of claim 148, wherein the cells

express nucleic acid encoding GIRK1 and GIRK4.

150. A method of claim 148 or 149, wherein the $GABA_BR1/R2$ receptor is a mammalian $GABA_BR1/R2$ receptor.

151. A method of screening a plurality of chemical compounds not known to inhibit the activation of a $GABA_BR1/R2$ receptor to identify a compound which inhibits the activation of the $GABA_BR1/R2$ receptor, which comprises:

(a) contacting cells containing nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, with the plurality of compounds in the presence of a known $GABA_BR1/R2$ receptor agonist, under conditions permitting activation of the $GABA_BR1/R2$ receptor;

(b) determining whether the activation of the $GABA_BR1/R2$ receptor is reduced in the presence of the plurality of compounds, relative to the activation of the $GABA_BR1/R2$ receptor in the absence of the plurality of compounds, and if it is reduced;

(c) separately determining the inhibition of activation of the $GABA_BR1/R2$ receptor for each compound included in the plurality of

compounds, so as to thereby identify the compound or compounds present in such a plurality of compounds which inhibits the activation of the $GABA_BR1/R2$ receptor.

152. The process of claim 151, wherein the cells express nucleic acid encoding GIRK1 and GIRK4.

153. A method of claim 151 or 152, wherein the $GABA_BR1/R2$ receptor is a mammalian $GABA_BR1/R2$ receptor.

154. A method of any one of claims 148, 149, 151, or 152, wherein the cell is a mammalian cell.

155. A method of claim 154, wherein the mammalian cell is non-neuronal in origin.

156. The method of claim 155, wherein the non-neuronal cell is a COS-7 cell, a 293 human embryonic kidney cell, a LM(tk-) cell or an NIH-3T3 cell.

157. A pharmaceutical composition comprising a compound identified by the method of claim 148 or 149, effective to increase $GABA_BR1/R2$ receptor activity and a pharmaceutically acceptable carrier.

158. A pharmaceutical composition comprising a compound

identified by the method of claim 151 or 152, effective to decrease $GABA_BR1/R2$ receptor activity and a pharmaceutically acceptable carrier.

159. A process for determining whether a chemical compound is a $GABA_BR1/R2$ receptor agonist, which comprises preparing a membrane fraction from cells which comprise nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, separately contacting the membrane fraction with both the chemical compound and GTPγS, and with only GTPγS, under conditions permitting the activation of the $GABA_BR1/R2$ receptor, and detecting GTPγS binding to the membrane fraction, an increase in GTPγS binding in the presence of the compound indicating that the chemical compound activates the $GABA_BR1/R2$ receptor.

160. A process for determining whether a chemical compound is a $GABA_BR1/R2$ receptor antagonist, which comprises preparing a membrane fraction from cells which comprise nucleic acid encoding and expressing on their cell surface the $GABA_BR1/R2$ receptor, wherein such cells do not normally express the $GABA_BR1/R2$ receptor, separately contacting the membrane fraction with the chemical compound, GTPγS and a second chemical compound known to activate the $GABA_BR1/R2$ receptor, with GTPγS and only the second compound, and with GTPγS alone, under conditions permitting the activation of the $GABA_BR1/R2$ receptor, detecting GTPγS binding to each membrane fraction, and comparing the increase in GTPγS binding in the presence of the

compound and the second compound relative to the binding of GTPγS alone, to the increase in GTPγS binding in the presence of the second chemical compound known to activate the $GABA_BR1/R2$ receptor relative to the binding of GTPγS alone, a smaller increase in GTPγS binding in the presence of the compound and the second compound indicating that the compound is a $GABA_BR1/R2$ receptor antagonist.

161. A process of claim 159 or 160, wherein the $GABA_BR2$ receptor is a mammalian $GABA_BR2$ receptor.

162. The process of claim 161, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by the plasmid BO-55 (ATCC Accession No. 209104).

163. The process of claim 162, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that shown in Figures 4A-4D (Seq. ID No. 4).

164. The process of claim 161, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has substantially the same amino acid sequence as that encoded by the plasmid pEXJT3T7-hGABAB2 (ATCC Accession No.).

165. The process of claim 161, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has

substantially the same amino acid sequence as that shown in Figures 23A-23D (Seq. ID No. 47).

166. The process of claim 161, wherein the $GABA_BR1/R2$ receptor comprises a $GABA_BR2$ polypeptide which has the sequence shown in Figures 23A-23D (Seq. ID No. 47).

167. The process of claim 159 or 160, wherein the cell is an insect cell.

168. The process of claim 159 or 160, wherein the cell is a mammalian cell.

169. The process of claim 168, wherein the mammalian cell is nonneuronal in origin.

170. The process of claim 169, wherein the nonneuronal cell is a COS-7 cell, CHO cell, 293 human embryonic kidney cell, NIH-3T3 cell or LM(tk-) cell.

171. The process of claim 170, wherein the compound was not previously known to be an agonist or antagonist of a $GABA_BR1/R2$ receptor.

172. A compound determined to be an agonist or antagonist of a $GABA_BR1/R2$ receptor by the process

of claim 171.

173. A method of treating spasticity in a subject which comprises administering to the subject an amount of a compound which is an agonist of a $GABA_BR1/R2$ receptor effective to treat spasticity in the subject.

174. A method of treating asthma in a subject which comprises administering to the subject an amount of a compound which is a $GABA_BR1/R2$ receptor agonist effective to treat asthma in the subject.

175. A method of treating incontinence in a subject which comprises administering to the subject an amount of a compound which is a $GABA_BR1/R2$ receptor agonist effective to treat incontinence in the subject.

176. A method of decreasing nociception in a subject which comprises administering to the subject an amount of a compound which is a $GABA_BR1/R2$ receptor agonist effective to decrease nociception in the subject.

177. A use of a $GABA_BR2$ agonist as an antitussive agent which comprises administering to the subject an amount of a compound which is a $GABA_BR1/R2$ receptor agonist effective as an antitussive agent in the subject.

178. A method of treating drug addiction in a subject which comprises administering to the subject an amount of a compound which is a $GABA_BR1/R2$ receptor agonist effective to treat drug addiction in the subject.

179. A method of treating Alzheimer's disease in a subject which comprises administering to the subject an amount of a compound which is a $GABA_BR1/R2$ receptor antagonist effective to treat Alzheimer's disease in the subject.

182. A process for making a composition of matter which specifically binds to a $GABA_BR1/R2$ receptor which comprises identifying a chemical compound using the process af any of claims, 82, 83, 99, 100, 114 or 115 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

183. A process for making a composition of matter which specifically binds to a $GABA_BR1/R2$ receptor which comprises identifying a chemical compound using the process of any of claims 120, 128, or 148 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

184. A process for making a composition of matter which specifically binds to a $GABA_BR1/R2$ receptor which comprises identifying a chemical compound using the process of any of claims 121, 130, or 151 and

then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

185. The process of any of claims 182, 183, or 184, wherein the $GABA_BR1/R2$ receptor is a human $GABA_BR1/R2$ receptor.

186. A process for preparing a pharmaceutical composition which comprises admixing a pharmaceutically acceptable carrier and a pharmaceutically acceptable amount of a chemical compound identified by the process of any of claims 82, 83, 99, 100, 114 or 115 or a novel structural and functional analog or homolog thereof.

187. A process for preparing a pharmaceutical composition which comprises admixing a pharmaceutically acceptable carrier and a pharmaceutically acceptable amount of a chemical compound identified by the process of any of claims 120, 128, or 148 or a novel structural and functional analog or homolog thereof.

188. A process for preparing a pharmaceutical composition which comprises admixing a pharmaceutically acceptable carrier and a pharmaceutically acceptable amount of a chemical compound identified by the process of any of claims 121, 130, or 151 or a novel structural and functional analog or homolog thereof.

189. The process of any of claims 186, 187, or 188, wherein the $GABA_BR1/R2$ receptor is a human $GABA_BR1/R2$. receptor.

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